Size at Birth, Maternal Weight, and Type 2 Diabetes in South India

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Recent research in Europe and the USA has shown that adults who had a low birthweight or who were thin at birth with a low ponderal index (birthweight/length^3) tend to be insulin resistant and have an increased risk of developing Type 2 diabetes mellitus. Low birthweight and Type 2 diabetes are common in India. We have studied glucose and insulin metabolism in 506 men and women (aged 39–60 years) born in a hospital in Mysore, South India, which kept detailed obstetric records from 1934. The prevalence of Type 2 diabetes was 15%. In contrast to Western populations, higher rates were found in men and women who were short at birth ($p = 0.07$) and had a high ponderal index ($p = 0.05$). Their mothers tended to be heavier than average during pregnancy ($p = 0.004$). Higher ponderal index at birth was also associated with a lower 30 minute insulin increment ($p = 0.009$), a marker of reduced beta cell function. We speculate that the rise in Type 2 diabetes in Indian urban populations may have been triggered by mild obesity in mothers, leading to glucose intolerance during pregnancy, macrosomic changes in the fetus, and insulin deficiency in adult life. © **1998 John Wiley & Sons, Ltd.**

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Introduction

Rates of Type 2 diabetes mellitus in people from the Indian sub-continent are among the highest in the world.[1,2] This was first shown in people who migrated from India and Pakistan to other countries;[1] in Britian their diabetes prevalence is up to five times that of the white indigenous population.[3,4] Although a large multi-centre study in 1975 reported a low prevalence of Type 2 diabetes in India itself,[5] and low rates of the disease persist in rural areas,[6] recent studies have shown high rates, comparable to those found in studies of migrants, in Indian cities.[6–9]

The 'epidemic' of Type 2 diabetes among urban Indians has been attributed to the presence of a 'thrifty genotype', which evolved to aid survival in subsistence conditions, but which leads to insulin resistance and diabetes in a modern setting of plentiful food supply, sedentary living, and obesity.[4] Recent research has suggested another explanation. Studies of adults whose size at birth was recorded have shown that reduced fetal growth and thinness at birth are associated with insulin resistance and high rates of Type 2 diabetes.[10–18] These findings have led to the 'thrifty phenotype' hypothesis,[19] that Type 2 diabetes is caused by undernutrition in fetal life. It is proposed that fetal undernutrition, which may result from maternal undernutrition or reduced transfer of nutrients to the fetus, permanently reduces the responsiveness to insulin of peripheral tissues.[19,20] Ageing, obesity, and physical inactivity in adult life contribute further to the development of disease. This model may explain the high levels of Type 2 diabetes in India, where maternal stunting and chronic energy deficiency, and poor fetal growth, are widespread.

To explore associations between size at birth and glucose and insulin metabolism we have studied men and women born in one hospital in Mysore, South India, where detailed obstetric records have been kept since 1934.

Subjects and Methods

The Holdsworth Memorial Hospital (HMH), Mysore, South India, was built in 1905 and for the first half of the century was one of three hospitals offering obstetric care in Mysore. From 1934 birthweight, crown–heel length and head circumference have been recorded routinely for babies born there. In addition, the obstetric records contain the parents' names, address, religion or caste and occupation, and the mother's obstetric history. They do not record gestational age. Most mothers who

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delivered in the hospital in the 1930s and 1940s came to the hospital for the first time in labour. Forty per cent attended the antenatal clinic during pregnancy, and their weights and urinalysis for sugar were recorded. The timing of their first visit ranged from the first trimester of pregnancy to the week before delivery (mean 13 weeks before delivery). External pelvic measurements, using obstetric callipers, were recorded for almost all primigravidae, and approximately half the multigravid mothers, when they were admitted in labour. They included intercristal (distance between iliac crests) and interspinous (distance between anterior superior iliac spines) diameters.

In total, 8883 singleton babies were born alive in HMH during 1934–1953. As previously described,[21] we traced 536 men and women born in the hospital, and 517 agreed to take part in the study. After a 12-h overnight fast they attended the hospital for a glucose tolerance test. Fasting blood samples were taken for measurement of plasma glucose, insulin, proinsulin, and 32–33 split proinsulin concentrations. Excluding people already known to have Type 2 diabetes, subjects were then given a 75 g oral glucose load and further blood samples taken for plasma glucose and insulin 30 and 120 min later. All except 11 subjects completed the test. Our analysis is limited to the 506 subjects who were either already known to have diabetes or who completed the glucose tolerance test.

The subjects' weight, height, waist, and hip circumferences were measured by one of two observers. Weight was measured to the nearest 0.5 kg using a portable Seca scale (CMS Instruments, London). Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (Microtoise, CMS Instruments, London), ensuring a level floor surface. Waist circumference was measured to the nearest 0.1 cm using a steel anthropometric tape midway between the costal margins and superior iliac crests, with the subject relaxed and in expiration. Hip circumference was measured as the maximum diameter at or around the level of the greater femoral trochanters. Information on socio-economic status was obtained by questionnaire using the Kuppuswamy score, a standardized questionnaire method for urban Indian populations, based on family size, type and location of housing, availability of water and sanitation, education, occupation, and income.[22] The fieldworkers were blind to the subjects' birth measurements.

Plasma glucose concentrations were measured in Mysore using a standard glucose oxidase method. Aliquots of plasma were stored in a −80 °C generator-protected freezer for up to 26 months, until the end of the study, and transported to the UK in dry ice. Plasma insulin, proinsulin, and 32–33 split proinsulin concentrations were measured at Addenbrooke's Hospital, Cambridge. Insulin was measured using the Medgenix immunoenzymometric assay (Medgenix SA, B-6220 Fleurus, Belgium). This assay did not cross-react with intact or 32–33 split proinsulin. Between-batch coefficients of variation were 11% at 24 pmol l^{-1}, 8 % at 60 pmol l^{-1}, and 4.8 % at 477 pmol l^{-1}. The 32–33 split proinsulin was measured using a two-site immunometric assay.[23,24] Intact proinsulin was measured using a microtitre plate time-resolved fluorescence (Delfia) assay. The solid phase and labelled antibodies used were the same monoclonal antibodies described for the immunoradiometric assay of intact proinsulin.[23,24] Tracer antibody was labelled with Europium using the Delfia Europium labelling kit 1244-302 (Wallac (UK) Ltd, Milton Keynes, Bucks, UK). This assay did not cross-react with insulin and 32–33 split proinsulin. Between-batch coefficients of variation were 10 % at 4.4 pmol l^{-1}, 5.8 % at 24 pmol l^{-1}, and 5.4 % at 86 pmol l^{-1}. Insulin assays were not carried out for four subjects known to be hepatitis B positive. In addition, fasting values for 10 subjects, 30-min values for 5 subjects, and 120-min values for 1-subject were not available, either because of difficulty with venesection or sample haemolysis.

Type 2 diabetes was defined as a 120-min glucose concentration of 11.1 mmol l^{-1} or more. Impaired glucose tolerance (IGT) was defined as a 120-min glucose concentration of 7.8–11.0 mmol l^{-1}.[25] Two variables were calculated from the glucose and insulin data. Relative insulin resistance calculated by homeostasis model assessment (RIR-HOMA) is a measure of insulin resistance.[26] It correlates well with insulin resistance measured by euglycaemic or hyperglycaemic clamp methods. The insulin increment ((insulin concentration at 30 min – fasting insulin concentration)/30-min glucose concentrations) is a measure of insulin secretion.[27,28] It correlates well with the first phase insulin release following intravenous glucose. The insulin increment and RIR-HOMA do not correlate with each other, and are useful as separate markers of insulin deficiency and resistance, both of which are thought to play a role in the pathogenesis of Type 2 diabetes.

Statistical Method

The birthweights of all 506 men and women were recorded. Birth length was recorded for 501 and head circumference at birth for 500. Maternal weight was recorded for 204 subjects, and pelvic dimensions for 280. Measurements were made in pounds and inches, and were often rounded, creating clumping of the data. For tabulations we have divided the measurements as closely as possible into thirds, and converted units to kilograms and centimetres. Plasma glucose, insulin, proinsulin and 32–33 split proinsulin concentrations and the insulin increment and RIR-HOMA had skewed distributions and were transformed to symmetry using logarithms. Data were analysed by multiple linear and logistic regression, using variables as continuous where appropriate.

Results

Table 1 shows the characteristics of the 506 Mysore men and women. Their age range was 39–60 years (mean 47). Two hundred and seventy-one (54 %) were Muslims, 182 (36 %) were Hindus, and 53 (10 %) were Christians. Two hundred and sixty-five (52 %) were upper socioeconomic class (Kuppuswamy groups I and II) and 241 (48 %) were lower class (groups III and IV).

Forty-two of the 506 subjects were already known to have Type 2 diabetes, and a further 33 were found to have diabetes, making the overall prevalence 15 %. The prevalence was similar in men (13 %) and women (16 %). It rose with age, from 12 % in people aged less than 50 years to 23 % in those aged 50 years or more. People with diabetes had a higher mean body mass index and waist/hip ratio. Upper class men and women had a higher prevalence (18 %) than lower class subjects (11 %) ($p = 0.03$). This difference was not statistically significant after allowing for body mass index ($p = 0.1$). Upper class men and women were taller than lower class subjects ($p < 0.01$ in both sexes), but the prevalence of diabetes was not related to adult height, either with or without adjustment for social class. The prevalence of diabetes was similar in the different religious groups. Ninety-seven (19 %) men and women were found to have IGT. As with diabetes, it was associated with age, obesity, and higher social class. Overall, 34 % of the subjects, and 46 % of those aged 50 or more, had abnormal glucose tolerance.

Table 2 shows mean plasma insulin, proinsulin, and 32–33 split proinsulin concentrations, and calculated RIR-HOMA and insulin increment, for the Mysore men and women. For comparison we have shown data from a population sample of British men and women of the same age (from the Ely Community Diabetes Project[29]). The Mysore men and women with normal glucose tolerance had higher fasting insulin, proinsulin, and 32–33 split proinsulin concentrations than the Ely men and women, despite being thinner. Their post-glucose insulin concentrations, and mean insulin increment, were also higher. Using linear regression we calculated predicted mean values for the Ely population for fasting, 30- and 120-min insulin, and intact and split proinsulin concentrations, adjusted to the lower body mass index of the Mysore population. The adjusted Ely means were lower than the observed means in Mysore ($p < 0.0001$ for all). Mysore subjects with diabetes also had high fasting values, but their 30-min insulin concentrations and mean insulin increment were low. Insulin variables

Table 2. Mean (SD) plasma insulin, proinsulin, 32–33 split proinsulin concentrations, RIR-HOMA and insulin increment in men and women in Mysore, India and Ely, UK

	Normal glucose tolerance		Impaired glucose tolerance	Type 2 diabetes
	Mysore	Ely, UK	Mysore	Mysore
Number	334	661	97	75
Body mass index (kg m^{-2})	22.7 (4.4)	25.4 (4.0)	26.4 (3.9)	25.2 (4.3)
Fasting insulin (pmol l^{-1})	41 (2.1[a])	39 (1.7[a])	77 (2.0[a])	90 (2.5[a])
30 min insulin (pmol l^{-1})	391 (1.9[a])	265 (1.8[a])	426 (2.3)[a]	238[b] (2.1[a])
120 min insulin (pmol l^{-1})	304 (2.2[a])	206 (1.9[a])	664 (2.1[a])	353[b] (2.2[a])
Proinsulin (pmol l^{-1})	5.3 (1.9[a])	3.3 (1.7[a])	10.4 (2.0[a])	16.3 (2.5[a])
32–33 split proinsulin (pmol l^{-1})	6.0 (2.2[a])	5.4 (1.9[a])	14.1 (2.3[a])	19.1 (2.8[a])
RIR-HOMA	1.7 (2.1[a])	1.8 (1.7[a])	3.9 (2.0[a])	7.4 (2.9[a])
Insulin increment	45 (1.9[a])	28 (2.0[a])	38 (2.2[a])	13[b] (3.0[a])

[a]Geometric mean and standard deviation.
[b]Data available for newly diagnosed diabetes only.

Table 1. Adult characteristics (mean (SD)) of the Mysore men and women

	Normal glucose tolerance		Impaired glucose tolerance		Type 2 diabetes		All		p[a]
	Men	Women	Men	Women	Men	Women	Men	Women	
Number	186	148	41	56	35	40	262	244	
Age (yr)	47 (5)	47 (5)	47 (5)	48 (5)	49 (5)	49 (4)	47 (5)	47 (5)	0.001
Weight (kg)	60 (11)	54 (12)	72 (12)	63 (12)	71 (16)	57 (10)	63 (13)	57 (12)	<0.0001
Height (m)	1.65 (0.06)	1.51 (0.06)	1.67 (0.06)	1.52 (0.07)	1.67 (0.06)	1.51 (0.06)	1.66 (0.06)	1.51 (0.06)	0.2
Body mass index (kg m^{-2})	21.8 (3.6)	23.8 (5.1)	25.6 (3.8)	26.9 (3.9)	25.3 (4.5)	25.1 (4.3)	22.9 (4.1)	24.7 (4.9)	<0.0001
Waist/hip ratio (%)	90 (6)	82 (6)	95 (5)	85 (5)	94 (6)	85 (5)	91 (6)	83 (6)	<0.0001
No. (%) Upper social class	84 (45)	71 (48)	28 (68)	34 (61)	26 (74)	22 (55)	138 (53)	127 (52)	men 0.0003 women 0.2

[a]p value for trend across the groups of glucose tolerance in a multiple linear regression analysis using three groups of glucose tolerance (normal, IGT, Type 2 DM) to predict each variable, allowing for sex. Trend in % upper social class assessed using a trend test for proportions.

rose with increasing body mass index ($p < 0.01$ for all). They rose with increasing age; these trends were statistically significant, independent of body mass index, for fasting insulin ($p = 0.05$), 32–33 split proinsulin ($p = 0.004$), proinsulin ($p = 0.0001$), and RIR-HOMA ($p = 0.0006$). Insulin concentrations were higher in women than men; the differences were statistically significant for fasting insulin ($p = 0.03$) and 120-min insulin ($p = 0.01$). Proinsulin ($p = 0.003$) and 32–33 split proinsulin (NS) concentrations were higher in men.

Type 2 Diabetes and Size at Birth

The subjects' mean (SD) birth measurements were: birthweight 2.75 (0.4) kg, birth length 47.9 (3.1) cm, head circumference 33.6 (1.7) cm and ponderal index (birthweight/length^3) 25.4 (4.9) kg m^{-3}. These are similar to current Indian community averages for term babies,[30] but small in all dimensions compared with babies born in the UK[31] (mean (SD) 3.46 (0.5), 50.1 (2.0), 35.1 (1.3), and 27.4 (2.3)). The deficit was greatest for birthweight. 29 % weighed 2.5 kg or less, and 96 % weighed less than 3.5 kg. Birthweight was correlated with adult body mass index ($r = +0.14$, $p = 0.001$) and birth length was correlated with adult height ($r = +0.13$, $p = 0.003$).

The prevalence of Type 2 diabetes was not related to birthweight ($p = 0.5$, $p = 0.9$ adjusted for age, sex, and body mass index). It fell with increasing birth length ($p = 0.1$, $p = 0.07$ adjusted), and rose with increasing ponderal index at birth ($p = 0.03$, $p = 0.05$ adjusted). Table 3 shows that the highest rates of diabetes were in men and women who were short at birth with a relatively high birthweight. In an analysis with birthweight and length together, adjusting for age, sex, and body mass index, diabetes prevalence was inversely related to birth length ($p = 0.05$) and positively, though not statistically significantly, related to birthweight ($p = 0.4$). Diabetes was not related to head circumference at birth.

The mothers of 204 (40 %) subjects attended the antenatal clinical. Their mean weight at first attendance was 47 (SD 8) kg. Urinalysis for sugar was negative in all. External pelvic diameters were recorded for 280 (55 %) mothers when admitted in labour. Mean (SD) intercristal and interspinous diameters were 24.5 (1.6) cm and 22.1 (1.5) cm, respectively. Table 4 shows that the prevalence of diabetes rose with increasing maternal weight and pelvic diameters. These trends remained statistically significant after allowing for the subjects' adult body mass index (Table 4), waist/hip ratio, and social class. Higher maternal weight and larger pelvic diameters were associated with increased birthweight ($p < 0.0001$) and ponderal index ($p < 0.05$), and, weakly, with increased birth length ($p = 0.09$ for maternal weight and interspinous diameter and $p = 0.2$ for intercristal diameter). The trends in diabetes prevalence with maternal weight and pelvic diameters remained after allowing for the subjects' birthweight, length or ponderal index. Maternal weight, and pelvic diameters rose with increasing maternal age ($p < 0.01$ for all) and parity ($p < 0.01$ for all). Allowing for these did not alter the trends in diabetes prevalence with maternal measurements.

Table 3. Percentages of subjects with Type 2 diabetes according to birthweight and length at birth

Birthweight (kg)	Birth length (cm)			
	≤46	–49	>49	All
≤2.5	11 (75)	8 (50)	11 (19)	10 (144)
–2.9	24 (80)	17 (64)	14 (56)	19 (200)
>2.9	23 (35)	14 (50)	11 (72)	15 (157)
All	18 (190)	13 (164)	12 (147)	15 (501)

Figures in parentheses are numbers of subjects.

Insulin Resistance and Size at Birth

Unadjusted values of fasting insulin, proinsulin, 32–33 split proinsulin, and RIR-HOMA were unrelated to size at birth. After adjusting for age, sex, and body mass index, fasting insulin, 32–33 split proinsulin, and RIR-HOMA were inversely related to birthweight ($p = 0.03$, 0.03 and 0.09, respectively). These associations were stronger in men ($p = 0.002$, 0.001, and 0.004) and not statistically significant in women ($p > 0.7$ for all). Table 5 shows the trends in fasting insulin concentrations with birthweight and adult body mass index. In men the highest concentrations were in those who had a low birthweight and high adult body mass index. In women the trends with both birthweight and body mass index were less. Interaction terms for birthweight and sex, and adult body mass index and sex, were both significantly related to fasting insulin ($p = 0.04$ and < 0.0001, respectively). There were similar findings for 32–33 split proinsulin and RIR-HOMA. The insulin resistance measures were not related to maternal weight or pelvic diameters.

Insulin Secretion and Size at Birth

The 30-min insulin concentrations and the insulin increment were not related to birthweight or length individually, but were lower in men and women who had a higher ponderal index at birth ($p = 0.03$) and 0.007). The trends were similar ($p = 0.03$ and 0.009, respectively) after allowing for age, sex, and body mass index. Table 6 shows that the mean insulin increment was low in people who had a short length at birth, and a relatively high birthweight. In a simultaneous regression analysis with age, sex, and body mass index, and birthweight and length together, mean insulin increment fell with decreasing length ($p = 0.05$) and increasing birthweight ($p = 0.009$). These trends were similar

Table 4. Percentages of men and women with Type 2 diabetes according to their mothers' measurements during pregnancy

	Men		Women		All	*p* for	*p* for
	n	% Diabetic	*n*	% Diabetic	% Diabetic	trend	trend[a]
Mothers' weight (kg)							
≤43	33	6	35	14	10		
–49	45	11	25	16	13		
>49	27	26	39	23	24		
All	105	13	99	18	16	0.0008	0.004
Mothers' intercristal diameter (cm)							
≤24	37	5	38	13	9		
–25	40	13	44	20	17		
>25	64	19	57	28	23		
All	141	13	139	22	18	0.009	0.02
Mothers' interspinous diameter (cm)							
≤21	33	3	31	6	5		
–22.5	40	15	42	24	20		
>22.5	68	18	66	27	22		
All	141	13	139	22	18	0.004	0.009

[a]Allowing for age, sex, and body mass index.

Table 5. Mean fasting insulin concentrations (pmol l^{-1}) according to birthweight and adult body mass index

Birthweight (kg)	Adult body mass index (kg m^{-2})			
	≤21	–24	>24	All
Men				
≤2.5	26 (37)	76 (22)	120 (8)	44 (67)
–2.9	33 (40)	70 (29)	111 (23)	57 (92)
>2.9	21 (29)	46 (35)	86 (28)	43 (92)
All	27 (106)	60 (86)	99 (59)	48 (251)
Women				
≥2.5	31 (27)	68 (22)	79 (28)	54 (77)
–2.9	34 (28)	49 (40)	74 (37)	51 (105)
>2.9	35 (10)	67 (17)	91 (32)	71 (59)
All	33 (65)	57 (79)	81 (97)	57 (241)

Figures in parentheses are numbers of subjects. Overall geometric S.D. = 2.3

Table 6. Mean insulin increment according to birthweight and birth length (people with Type 2 diabetes excluded)

Birthweight (kg)	Birth length (cm)			
	≤46	–49	>49	All
≥2.5	46 (62)	41 (43)	64 (17)	46 (122)
–2.9	39 (60)	47 (51)	48 (46)	44 (157)
>2.9	33 (24)	49 (41)	39 (61)	41 (126)
All	41 (146)	46 (135)	45 (124)	44 (405)

Figures in parentheses are numbers of subjects. Overall geometric S.D. = 2.0

($p = 0.07$ and 0.007) if subjects with diabetes were excluded. Mean insulin increment was lower in people whose mothers were heavier ($p = 0.2$) or had larger intercristal ($p = 0.04$) and interspinous ($p = 0.03$) diameters.

We examined the effect on plasma insulin, proinsulin, and 32–33 split proinsulin concentrations of storage time before laboratory analysis. There were no trends in insulin or proinsulin concentrations with time, but there was a significant trend in 32–33 split proinsulin concentrations ($p = 0.01$), which fell by an average 2.5 % per month of storage. Adjustment for storage time, however, did not alter the relationships reported above.

Discussion

We have studied glucose and insulin metabolism in a sample of men and women who were born in Mysore, South India, 40 or more years ago, and still live in the city. Consistent with other recent studies in India,[6–9] their prevalence rates of Type 2 diabetes (15 %) and IGT (19 %) were high (Table 1). Diabetes was associated with known adult risk factors for the disease, including age and obesity.

The Mysore men and women were similar in size at birth to Indian babies born today,[30] but very different from babies born in the West. They were shorter and lighter, the deficit being greatest for birthweight; 96 % were below the mean UK birthweight of 3.5 kg. Studies in Europe and the USA[10–12,14–18] have shown that Type 2 diabetes is associated with low birthweight and ponderal index at birth. In marked contrast, in Mysore, people with the highest rates of diabetes were short at birth, with a relatively high ponderal index (Table 3). The prevalence of Type 2 diabetes was increased in people whose mothers had a relatively high pregnancy weight and large pelvic diameters (Table 4). These associations were strong, despite the fact that maternal weight was available for only half of our subjects, and weight was measured at varying intervals before birth. They were independent of the subjects' age, obesity, and social class, and of the mothers' age and parity.

This strong link between higher maternal weight and pelvic diameters, and Type 2 diabetes, can be interpreted only tentatively. Higher weight in pregnancy may reflect greater stature, fatness or lean body mass. External pelvic measurements do not correlate with height,[32] and are known to increase during pregnancy.[33] In Mysore they increased with parity and with maternal age, beyond the age of skeletal maturity. This suggests that they reflect maternal subcutaneous fat as well as bony diameters. We conclude that the relationship of Type 2 diabetes to maternal size reflects an association with maternal adiposity.

Insulin concentrations showed that, like other Indian populations,[4] the Mysore men and women were insulin resistant, despite low levels of obesity. Subjects with diabetes had a low insulin increment, suggesting that in addition to insulin resistance, they had impaired insulin secretion. The data suggest that in this population there were two neonatal phenotypes associated with abnormal adult insulin metabolism. Lower birthweight babies developed insulin resistance, but were apparently able to maintain a high insulin output. Babies who were short, with a high ponderal index, developed impaired insulin secretion and diabetes. There is likely to be overlap between these phenotypes, as many of the latter, despite a high ponderal index still had a relatively low birthweight. They may have undergone a period of insulin hypersecretion before β-cell dysfunction occurred.

One interpretation of our data is that this population is intrinsically different from Western populations, with different associations between fetal growth and adult diabetes. We propose, however, the following hypothesis to make sense of our findings in the context of data from other populations (Figure 1). We suggest that insulin resistance is widespread in India, especially among low birthweight people. This is exacerbated if people become even mildly obese or less physically active, changes which accompany urbanization. This increase in insulin resistance leads to the development of glucose intolerance in pregnant women, which is rare in rural areas of India. It is known that maternal hyperglycaemia, even within the 'normal' range, is associated with increased fatness (macrosomia), without increased length, in the baby.[34] Gestational diabetes in humans,[35,36] and experimentally induced hyperglycaemia during pregnancy in animals[37–39] are associated with diabetes in the adult offspring. The animal evidence suggests that this is due to insulin deficiency. We speculate that the rise in Type 2 diabetes in urban Indian populations may have been triggered by glucose intolerance during pregnancy in insulin-resistant mothers who became less physically active and mildly obese in adult life.

The men and women we studied were born in one hospital, survived into adult life, were identified in our survey, and gave sufficient information for us to match them with certainty to their birth records. The majority of births at that time took place either at home or in the city's government hospital. Many babies would have

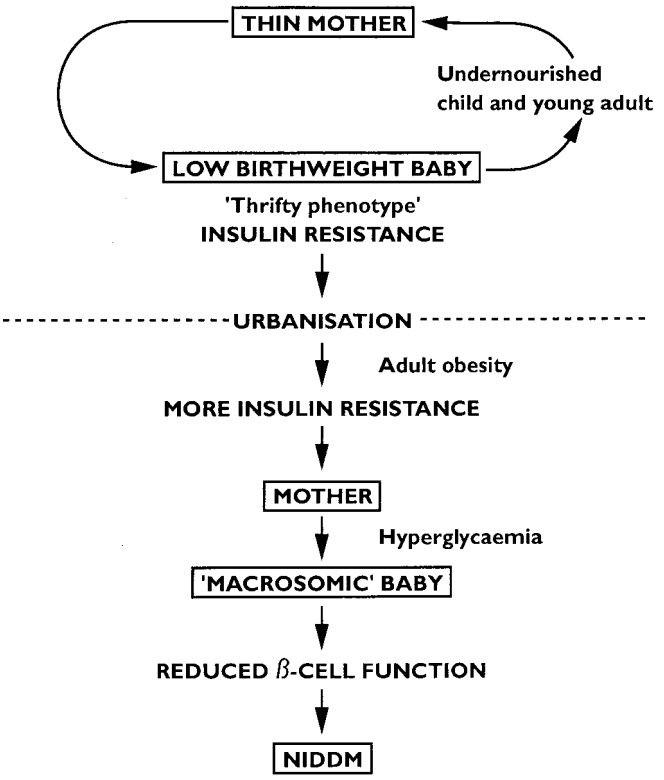

Figure 1. Hypothesis derived from findings: Type 2 diabetes triggered by increasing insulin resistance and glucose intolerance in mothers during pregnancy

died in infancy and childhood. Our sample was only 6 % of all births in HMH between 1934 and 1953. For practical reasons we traced people still living within 2 miles of the hospital, and our sample is not representative of the entire population of modern Mysore. Their anthropometric data, however, were similar to those recorded for men and women of the same age in a recent urban population study in South India.[40] Our analysis was based on internal comparisons, and unrepresentativeness of our sample would only introduce bias if the associations between ponderal index and diabetes differed in those born in and outside the hospital, and in those traced and not traced. This is possible, for example, if our sample contained more people in nutritional transition than people whose nutrition and lifestyle had been stable across recent generations. Our findings will need to be confirmed in other Indian populations.

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